The Examiner has indicated that he has considered the Preliminary Amendment we filed on June 27, 2000, and has withdrawn the Office Action and Advisory Action incorrectly issued on July 6, 2000 and December 4, 2001. Applicants appreciate the clarification.

Written Description Rejection

The Examiner has maintained his written description rejection of claims 23-25. The Examiner believes that the invention as claimed is broadly directed to purified HIV-1 variants that differ genetically in the *gag*, *pol*, and *env* coding regions from three known HIV-1 prototypes (IIIB, BRU, and ARV-2) by the specified amounts (at least 3.4% in Gag, 3.1% in Pol, and 13.0% in Env). Further limitations state that AIDS patient antibodies also bind to the Gag, Pol, or Env polypeptides of the HIV-1 variants and the same polypeptides in HIV-1_{MAL}. The Examiner states that this encompasses a large genus of genotypically/phenotypically unrelated HIV strains.

Turning to the specification, the Examiner believes that it only describes the molecular cloning and characterization of a single novel HIV-1 isolate, LAV-1_{MAL}. The Examiner believes that the skilled artisan would not have reasonably concluded that the inventors were in possession of any other HIV-1 variant. The Examiner states that the specification does not provide information on the isolation, characterization, and nucleotide sequence for any other HIV-1 variants.

In response to this rejection, Applicants filed a continuation application with a Preliminary Amendment and the Declaration of Mme. Denise Guétard. The Preliminary

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Amendment and Declaration both argued that the specification supports claims to both HIV-1_{MAL} and HIV-1_{ELI}, as well as a broader genus of viruses. Applicants pointed out the derivation of the HIV-1_{ELI} strain from a patient in Zaire. Applicants also stated that the specification provides the amino acid sequences for particular proteins from HIV-1_{ELI}. Additionally, Applicants pointed to the comparison of amino acid sequences between HIV-1_{ELI}, HIV-1_{MAL}, and other HIV-1 strains.

Next, Applicants stated that these two strains HIV-1_{ELI} and HIV-1_{MAL} differed from other HIV-1 strains, such as HIV-1_{BRU} and HIV-1_{ARV-2}. Applicants argued that these viruses were evolutionarily related as diverging from a common origin. Thus, Applicants argued that Applicants had invented a class of evolutionarily related viruses. It is this class of viruses that is being claimed in this application.

The Examiner considered the Preliminary Amendment and the Declaration of Mme. Guétard and has indicated he believes that the claimed invention is not supported by the written description in the specification. The Examiner makes several specific points maintaining his rejection of the claimed invention.

First, the Examiner argues that the application only describes the cloning and characterization of HIV-1_{MAL}. In response, Applicants wish to point out that the application provides the amino acid sequence and deposit information on HIV-1_{ELI}, showing that this virus was in possession of the inventors. (Specification, figure 3 and page 37, lines 13-15, respectively). As the application claims a class of viruses, not a viral DNA sequence, it is not necessary to have provided the DNA sequence of the

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virus. A description of the virus and a deposit are sufficient to show that the HIV-1_{ELI} virus was in the possession of the inventors.

Second, the Examiner argues that there are errors in the sequence comparisons defining the genus of claims. The Examiner argues that the claim limitations of sequence variation of greater than 3.4%, 3.1%, and 13.0% for *gag*, *pol*, and *env* do not agree with the sequence comparisons in Figures 3 and 4, which show that HIV-1_{MAL} and HIV-1_{ELI} differ from HIV-1_{BRU} by 20.7% and 21.7% in *env*, 9.8% and 12.0% in *gag*, and 5.5% and 7.7% in *pol*. The Examiner asserts that the percentages in the claims are actually derived from a sequence comparison between HIV-1_{BRU} and HIV-1_{ARV-2}.

The specification explains that HIV-1_{ELI} and HIV-1_{MAL} are more divergent from HIV-1_{BRU}, than HTLV-3 and HIV-1_{ARV-2} are from HIV-1_{BRU}. Thus, the percentages provided in the specification are correct as they define the class of viruses that are more divergent from HIV-1_{BRU} than both HTLV-3 and HIV-1_{ARV-2}. (Specification, page 10, lines 18-20). Additionally, Applicants wish to point out that viral conserved genomes generally have less than 1% variation in sequence. *See* Virology, Chapter 7, Mutation: Spontaneous Mutation, pages 102-103 (B.N. Fields, ed. 1985) (relevant pages enclosed). Nevertheless, Applicants have added claims 39-41, however, to viruses that differ from HIV-1_{BRU} by at least 20.7% in *env*, 9.8% in *gag*, and 5.5% in *pol*, basing the percentages on HIV-1_{ELI}, the less divergent of the two enumerated viruses in this class.

Third, the Examiner argues that even if the inventors had described the characterization and cloning of two HIV-1 species, it would be insufficient to support the allegedly broad genus claimed. This application defines the genus of viruses by

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providing specific examples of two species along with a structural description common to the class. Again, the Examiner focuses in this section of the Office Action on the written description and conception case law related to DNA sequences. Applicants, however, are not claiming a DNA sequence, or group of DNA sequences; instead Applicants are claiming a group of viruses with a common structural feature. The claims define the common structural feature of a certain amount of amino acid sequence variation from HIV-1_{BRU} and that feature is common to all members of the genus. Again, the amount of variation is unusual, as conserved viral genomes generally have only about 1% variation.

Turning to the case law of written description, the written description requirement can be satisfied by either the "recitation of a representative number of [species] . . . falling within the scope of the genus or a recitation of structural features common to the members of the genus." *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). This case continues by quoting an earlier case, stating that describing one member of a genus is not sufficient, but "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by other appropriate language." *Id.* (citations and quotations omitted).

Thus, Applicants believe that the genus in question is supported by the written description of the specification, both because two enumerated species are provided and because structural features of the genus are also defined. Applicants, thus, request that the Examiner withdraw this rejection. Alternatively, Applicants request that the Examiner allow claims 39-41 as drawn to a narrower embodiment of the invention.

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Anticipation and Obviousness Rejections

The Examiner has rejected claims 23-25 as anticipated, or in the alternative, obvious over *Myers*. *Myers* allegedly provides the complete nucleotide sequence of a novel purified HIV-1 isolate designated Z2Z6. The isolate is genetically related to the HIV-1 isolates ELI and MAL and appears to be only distantly related to the isolates BRU, IIIB (or HXB2), and ARV-2 (SF-2). The Examiner believes that this isolate varies from BRU, IIIB, and ARV-2 by at least 3.4%, 3.1%, and 13.0% in the *gag*, *pol*, and *env* coding regions, respectively. Thus, the Examiner believes that this isolate meets all of the limitations of the claimed invention. Further, due to the close genetic relationship between Z2Z6 and the isolates ELI and MAL, the Examiner alleges that the skilled artisan would reasonably expect nucleic acid probes and antibodies specific for MAL to also recognize Z2Z6 nucleic acids and antigens.

Myers was published after the U.S. and French priority dates (U.S. Appln. Ser. No. 07/038,330, filed April 13, 1987, and French Appln. 86401380.0, filed June 23, 1986). Applicants have argued that the specification fulfills the written description requirement and, thus, the *Myers* article, published in 1990, cannot be prior art.

Applicants request that the Examiner withdraw this rejection.

Conclusion

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 23-25 and 39-41 in condition for allowance. Applicants submit that the proposed amendments of claims 39-41 do not raise new

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issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicants respectfully point out that the final action by the Examiner presented some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the entering of the Amendment would allow the Applicants to reply to the final rejections and place the application in condition for allowance.

Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicants submit that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: January 8, 2003

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